

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Attention Deficit–Hyperactivity Disorder in Children and Adolescents

Heidi M. Feldman, M.D., Ph.D., and Michael I. Reiff, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

From the Department of Pediatrics, Stanford University School of Medicine, Stanford, CA (H.M.F.); and the Department of Pediatrics, University of Minnesota, Minneapolis (M.I.R.). Address reprint requests to Dr. Feldman at the Department of Pediatrics, Stanford University School of Medicine, 750 Welch Rd., Suite 315, Palo Alto, CA 94304, or at hfeldman@stanford.edu.

N Engl J Med 2014;370:838–46.

DOI: 10.1056/NEJMcpl307215

Copyright © 2014 Massachusetts Medical Society.

A 9-year-old boy who received a diagnosis of attention deficit–hyperactivity disorder (ADHD) at 7 years of age is brought to your office by his parents for a follow-up visit. He had had behavioral problems since preschool, including excessive fidgeting and difficulty following directions and taking turns with peers. Parent and teacher ratings of behavior confirmed elevated levels of inattention, hyperactivity, and impulsivity that were associated with poor grades, disruptions of classroom activities, and poor peer relationships. He was treated with sustained-release methylphenidate. Although parent and teacher rating scales after treatment showed reduced symptoms, he still makes many careless mistakes and has poor grades and no friends. What would you advise?

THE CLINICAL PROBLEM

ADHD in children is characterized by inattention, hyperactivity, impulsivity, or a combination of these symptoms, which compromise basic everyday functions such as learning to read and making friends.^{1,2} In the absence of biomarkers, diagnostic criteria focus on behavioral symptoms. Since the same characteristics may be observed in children and adolescents during typical development, the diagnosis of ADHD calls for symptoms that are severe, out of proportion to expectations according to the child's age or developmental level, and persistent and for which there are no appropriate alternative explanations. The disorder is typically diagnosed in childhood, but affected persons frequently remain symptomatic into adulthood.³ ADHD is associated with low rates of high-school graduation and completion of postsecondary education⁴ and poor peer relationships,⁵ even when it is appropriately managed,⁶ leading to high economic and social burdens.^{7,8}

ADHD is the most prevalent neurodevelopmental disorder among children. In the United States, approximately 5.4 million children between 6 and 17 years of age (9.5% of all U.S. children) have received an ADHD diagnosis.⁹ The prevalence of this condition increased by 33% between 1997–1999 and 2006–2008.¹⁰ High prevalence rates suggest overdiagnosis. Studies of regional variation in the United States have shown that higher prevalence is associated with increased physician supply,¹¹ and total sales of medications to treat ADHD have soared with marketing to physicians and directly to the general public¹² — findings that are consistent with overdiagnosis or overreporting. However, there are also indications of underdiagnosis. Children with disruptive and hyperactive behaviors are the most likely to be referred for clinical evaluation, and in children who do not have these behaviors, ADHD may remain unidentified or untreated.^{13,14} In community-based samples, the prevalence of this condition is higher among boys than among girls, and more boys than girls have a combination of inattention and hyperactivity rather than inattention alone.



An audio version
of this article is
available at
NEJM.org

KEY CLINICAL POINTS

ATTENTION DEFICIT–HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS

- Attention deficit–hyperactivity disorder (ADHD), the most prevalent neurobehavioral disorder in children, is associated with adverse long-term functional outcomes.
- Diagnostic evaluation relies on the use of validated parent and teacher rating scales that assess the child's behavior in everyday situations in various environments. Adolescents provide self-report as part of the diagnostic evaluation.
- Coexisting conditions and problems, especially learning disorders, anxiety and depression (internalizing disorders), and oppositional behaviors and conduct disturbance (externalizing disorders), must be considered in the evaluation and management of ADHD.
- Treatment should address a child's areas of functional disability rather than focus exclusively on ADHD core symptoms. Management plans developed with the child and family members, including parents, should specify measurable target objectives that relate to broader functional outcomes and are monitored in the evaluation of treatment effectiveness.
- Stimulant medications reduce the symptoms of ADHD without necessarily improving corresponding functional limitations.
- Behavior management is not as effective as medication in reducing core symptoms, but it improves functioning, which is important for subgroups of children with ADHD, and it increases parental satisfaction.

An international meta-regression analysis showed an aggregate prevalence of ADHD of 5.3% (95% confidence interval, 5.0 to 5.6); variations in prevalence were related to diagnostic criteria. The prevalence in Africa and the Middle East is lower than in other regions of the world.¹⁵

CLASSIFICATION

In community-based samples, among children who do not meet diagnostic criteria for ADHD, symptoms of inattention and overactivity correlate inversely with academic performance^{16,17}; this finding indicates that the severity threshold in this disorder is arbitrary. Criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) of the American Psychiatric Association guide diagnosis in the United States.^{1,2} The criteria in the fifth and most recent version, the DSM-5, which was released in May 2013, have not changed substantially from those of the DSM-IV. In both editions, the diagnosis in children is based on the presence of at least six of nine symptoms in either or both of two domains: inattention and hyperactivity–impulsivity. The DSM-5 differs from the previous edition in that adolescents and adults must present with at least five symptoms in either or both of the two domains, symptoms must be present before 12 years of age, and the diagnosis of ADHD can be made in persons who also have a diagnosis of autism

spectrum disorder.² A section of the DSM-5 on risks and prognostic factors emphasizes the need to take into account the child's environmental circumstances. Long-term life stressors such as poverty and physical or emotional abuse may lead to symptoms similar to ADHD or may increase the severity of ADHD symptoms.

The *International Classification of Diseases*, 10th edition (ICD-10),¹⁸ uses the alternative term “hyperkinetic disorder.” A diagnosis of ADHD according to this classification requires the presence of both impaired attention and activity problems¹⁹; thus, there is a lower prevalence of ADHD according to the ICD-10 criteria than according to the DSM-5 criteria (Table 1).

PATHOGENESIS AND RISK FACTORS

Family, twin, and adoption studies provide evidence that ADHD has a genetic component. Heritability has been estimated at 76%.²⁰ Meta-analyses of candidate-gene association studies have shown strong associations between ADHD and several genes involved in dopamine and serotonin pathways.²⁰ Multiple genes, each with a small effect, may together mediate genetic vulnerability. Nongenetic factors (e.g., maternal smoking during pregnancy or exposure to environmental lead or polychlorinated biphenyls) may also interact with genetic predisposition in the pathogenesis of ADHD.^{21,22}

Table 1. Criteria for the Diagnosis of Attention Deficit–Hyperactivity Disorder (ADHD) and Hyperkinetic Disorder.

Criteria	DSM-IV*	DSM-5†	ICD-10‡
Symptoms			
Inattention	Six of nine symptoms	Six of nine symptoms in children; five of nine symptoms in adolescents and adults (≥17 yr)	Three of five symptoms
Hyperactivity and impulsivity	Six of nine symptoms	Six of nine symptoms in children; five of nine symptoms in adolescents and adults (≥17 yr)	Three of five symptoms of hyperactivity and one of four symptoms of impulsivity
Age at onset	<7 yr	<12 yr	<7 yr
Settings	Either inattention or hyperactivity–impulsivity in ≥2 settings	≥2 settings	Inattention and hyperactivity at home and school
Duration	≥6 mo	≥6 mo	≥6 mo
Impairment	Clinically significant impairment in social, academic, or occupational functioning	Interference with functioning or development; specify mild, moderate, or severe functional impairment or symptoms	Clinically significant distress or impairment in social, academic, or occupational functioning
Subtypes	ADHD: combined type (inattentive and hyperactive–impulsive), predominantly inattentive type, or predominantly hyperactive type	ADHD: combined inattentive and hyperactive–impulsive presentation, predominantly inattentive presentation, or predominantly hyperactive–impulsive presentation	Hyperkinetic syndrome, hyperkinetic conduct disorder, or other hyperkinetic disorders

* The criteria are based on the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV).¹

† The criteria are based on the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5).²

‡ The criteria are based on the *International Classification of Diseases*, 10th edition (ICD-10).¹⁹

Neuroimaging studies have shown that ADHD is associated with a delay in cortical maturation.²³ ADHD has long been thought to reflect dysfunction of prefrontal–striatal circuitry.²⁴ Recent studies suggest that the pathophysiological features also encompass large-scale neural networks, including frontal-to-parietal cortical connections.²⁵ However, measures of brain structure and function in persons with ADHD overlap substantially with those of the general population and thus are not useful in diagnosis.

STRATEGIES AND EVIDENCE

DIAGNOSIS

Core symptoms that are diagnostic of ADHD are not always observed in children in the clinical setting. Therefore, parents, teachers, and others with knowledge of the child must provide information about the child's symptoms in everyday situations. In adolescents, self-report is an additional element in assessment because overt symptoms of inattention and hyperactivity subside and adult observers cannot judge the internal challenges to maintaining attention or stillness. Quantification of behavioral traits with the use of reliable, validated rating scales is impor-

tant to document the severity of symptoms before and after the initiation of treatment (see Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).

Other medical and psychosocial conditions with manifestations similar to those of ADHD should be considered in the diagnostic process. These conditions include seizure disorders, sequelae of central nervous system trauma or infection, sleep disorders, hyperthyroidism, physical or sexual abuse, and substance abuse. However, no medical, psychological, or neuropsychological tests are required to establish the diagnosis unless relevant signs or symptoms are noted in the history or physical examination.²⁶

ADHD frequently presents with other conditions and problems, primarily learning and language disorders, oppositional behavior and conduct disturbance (externalizing disorders), anxiety and depression (internalizing disorders), and coordination difficulties.²⁶ ADHD may also accompany autism, the fragile X syndrome, epilepsy, traumatic brain injury, Tourette's syndrome, and sleep disturbance. The diagnostic process should identify any coexisting conditions to modify the management plan accordingly.

The *International Classification of Functioning, Dis-*

ability and Health^{27,28} provides a systematic approach for cataloguing the range of functional consequences of ADHD and coexisting conditions with respect to body function and structures, activities of daily living, and participation in the community.^{4,29} Specific functions that may be impaired in ADHD are listed in Figure 1 in the Supplementary Appendix. Functional assessment at the time of diagnosis is useful for documenting the type and extent of functional difficulties and identifying meaningful goals for management.

MANAGEMENT

ADHD is a long-term condition. As such, treatment should take place within a medical home,^{30,31} where the health care team collaborates and coordinates with the family, other health and mental health clinicians, educators, and the patient to develop comprehensive plans that address symptoms and function over time. Management plans should specify measurable target objectives that relate to broader functional outcomes and that guide the evaluation of treatment effectiveness.²⁶ Objectives may include quantifiable increases in academic accuracy and productivity, prosocial behaviors, and decreased classroom disruptions.

Medications

Short-term randomized, placebo-controlled trials (generally <4 months in duration) involving children with ADHD have shown a clinically significant benefit of stimulant medications (derived from methylphenidate or amphetamines) in reducing inattention, hyperactivity, and impulsivity.³²⁻³⁴ Comparative-effectiveness studies have shown that various stimulants are similar in terms of effect size and adverse-effect profiles, though individual patients may have greater positive effects, fewer adverse effects, or both with particular medications than with others.^{33,35} Sustained-release and long-acting preparations of stimulant medications are generally preferred over short-acting agents because they allow administration of a single morning dose to improve symptoms for the entire school day without increasing adverse effects. Table 2 lists medications for the treatment of ADHD, their recommended doses, and potential adverse effects. The two most common side effects are appetite suppression and delayed onset of sleep.

One selective norepinephrine-reuptake inhibitor (atomoxetine) and two selective α_2 -adrenergic ago-

nists (extended-release guanfacine and extended-release clonidine) have been shown to be effective in reducing core symptoms in short-term placebo-controlled clinical trials, but they have weaker effects than those reported with stimulants (Table 2).³⁶ Nonstimulant medications play an important role in the management of ADHD when parents do not want their children to receive stimulants, when stimulants are contraindicated or have adverse effects, or when there is a history or high likelihood of addiction or diversion of medication for recreational use.

Behavioral Therapy

Behavioral therapy is central to the management of ADHD.³⁷ Efficacy has been established in clinical trials, crossover studies, and studies with single-subject designs.³⁷ Behavioral therapies enhance motivation by using rewards and other consequences and by providing models and opportunities for social learning.³⁸ Parental training in behavioral management (called “behavioral parent training”) is a systematic approach that teaches parents to shape their child’s behaviors with the use of the basic principles of behavior modification and social learning theory (Table 3). Program features associated with better outcomes include teaching parents how to communicate about their emotions, promoting positive parent-child interaction skills, and requiring parents to practice applying behavior-modification techniques with their children during training sessions.³⁹ Behavioral peer interventions that have been found to be effective in randomized clinical trials involve daylong, intensive social-skills training in natural settings such as summer school. Peer interventions are often instituted concurrently with behavioral parent training.³⁷

In nonrandomized studies, behavioral classroom management at school has been associated with moderate-to-large improvements in academic and behavioral functioning in children with ADHD (Table 3).⁴⁰ School-based strategies have been successful in positive environments where punishment is minimized.⁴⁰ Because ADHD is a disability, U.S. schools can provide accommodations, including behavior-management services, for children with this disorder under section 504 of the Rehabilitation Act of 1973. ADHD is not an eligibility category for special-education services under the Individuals with Disabilities Education Act. Children with ADHD may be eligible for an individualized educational

Table 2. Pharmacotherapeutic Agents for the Treatment of ADHD in Children and Adolescents.*

Medication and Trade Name	Dose	Duration of Effect <i>hr</i>	Common Side Effects	Uncommon Side Effects
Amphetamine stimulants				
Mixed amphetamine salts				
Adderall	2.5–5 mg once or twice daily, to a maximum of 40 mg	6	Headache, abdominal pain, decreased appetite, delayed onset of sleep	Tics, deceleration in rate of growth, agitation or anxiety, increased heart rate or blood pressure
Adderall XR	5 mg/day, to a maximum of 40 mg	10		
Dextroamphetamine				
Dexedrine or Dextrostat	2.5 mg two or three times a day, to a maximum of 40 mg	4–6		
Dexedrine Spansule	5 mg once or twice daily, to a maximum of 40 mg	≥6		
Lisdexamfetamine: Vyvanse	20 mg/day, to a maximum of 70 mg	10–12		
Methylphenidate stimulants				
Methylphenidate				
Concerta	18 mg/day, to a maximum of 72 mg	12		
Methylin	5 mg two or three times a day, to a maximum of 60 mg	3–5		
Daytrana transdermal patch	10 mg (apply for 9 hr), to a maximum of 30 mg	11–12		
Ritalin	5 mg two or three times a day, to a maximum of 60 mg	3–5		
Ritalin LA	20 mg/day, to a maximum of 60 mg	6–8		
Ritalin SR	20 mg once or twice daily, to a maximum of 60 mg	2–6		
Metadate CD	20 mg/day, to a maximum of 60 mg	6–8		
Quillivant XR	25 mg/5 ml/day, to a maximum of 60 mg	5		
Dermethylphenidate				
Focalin	2.5 mg twice daily, to a maximum of 60 mg	3–5		
Focalin XR	5 mg/day, to a maximum of 20 mg	8–12		
Norepinephrine-reuptake inhibitor (atomoxetine): Strattera	0.5 mg/kg/day once or twice daily, to a maximum of 1.4 mg/kg	At least 10–12	Upset stomach, decreased appetite, dizziness, fatigue, nausea, mood swings	Jaundice and liver involvement, suicidal ideation, slowed rate of growth, allergic reactions, priapism
α₂-Adrenergic agonists				
Extended-release guanfacine: Intuniv				
Extended-release clonidine: Kapvay	1 mg/day, to a maximum of 4 mg/day 0.1 mg once or twice daily, to a maximum of 0.4 mg/day	At least 10–12 At least 10–12	Somnolence and sedation, trouble sleeping, fatigue, headache, dry mouth, constipation, nausea, abdominal pain Somnolence and sedation, fatigue, insomnia, nightmares, dizziness, dry mouth, symptoms of upper respiratory tract infection	Hypotension, cardiac conduction abnormalities, seizures, chest pain, allergic reaction Cardiac conduction abnormalities, mood changes, allergic reaction

* All agents listed have been approved by the Food and Drug Administration for use in children and adolescents. Data are from Subcommittee on Attention-Deficit/Hyperactivity Disorder Steering Committee on Quality Improvement Management.³⁶

program under other criteria (such as “other health impairment” or “specific learning disability”) if their symptoms interfere with learning.

The Multimodal Treatment of ADHD Study (MTA), the longest trial of ADHD treatment (14 months), compared the use of medication (with monthly visits after the initial dose adjustment), intensive behavioral therapy, the combination of medical and behavioral therapy, and community-based care in children who were 7.0 to 9.9 years of age at study entry.⁴¹ Symptoms improved after treatment in all groups. Medication (predominantly methylphenidate hydrochloride) was superior to behavioral therapy for reducing the core symptoms of ADHD; the combination of medical and behavioral therapy was not significantly more effective than medication alone for these symptoms. Secondary analyses showed that, as compared with medication alone, combined therapy resulted in greater improvements in academic performance and reductions in conduct problems, higher levels of parental satisfaction, and the use of lower doses of stimulant medication. Combined therapy was also superior for treating children of low socioeconomic status and those with coexisting anxiety.⁴²

TREATMENT OF PRESCHOOL CHILDREN

The medical treatment of preschoolers with ADHD is controversial. An 8-week randomized, placebo-controlled trial of medication (the Preschool ADHD Treatment Study) enrolled preschoolers who remained symptomatic after their parents had received required behavior-management training.⁴³ Stimulant medication improved symptoms. The American Academy of Pediatrics (AAP) recommends that behavior management precede any consideration of medication for preschoolers.^{26,36}

LONGITUDINAL CARE

The AAP recommends monthly visits for adjusting medication in children and adolescents with ADHD, followed by at least semiannual visits until steady progress toward behavioral and functional goals has been achieved.³⁶ Follow-up care requires monitoring of symptoms, concurrent conditions, measurable objectives, and general functional outcomes. Routine monitoring in children receiving medication should include measurements of height, weight, blood pressure, and heart rate. Adverse reactions may change over time and should be assessed routinely. The dura-

Table 3. Behavioral Treatments for Children and Adolescents with ADHD.

Intervention	Description	Expected Outcomes	Effect Size	Factors Associated with Good Outcomes	Reference
Behavioral parent training	Behavior-modification principles provided to parents for use at home	Improved compliance with commands and parental understanding of behavioral principles; high level of parental satisfaction with treatment	Moderate	Parents learn how to use “time out” correctly, respond consistently to and interact positively with their child; requires parents to practice with their child during program sessions	Centers for Disease Control and Prevention ³⁹
Behavioral classroom management	Behavior-modification principles provided to teachers for use in classrooms; based on behavioral therapy principles and self-regulation interventions	Improved attention to instruction, compliance with classroom rules, decreased disruptive behavior, and improved work productivity	Moderate	Programs tailored to meet individual students’ needs and delivered in a positively reinforcing environment with minimal use of punitive strategies	DuPaul et al. ⁴⁰
Behavioral peer interventions	Interventions focused on peer relationships; these are often group-based interventions provided weekly and include clinic-based social-skills training used either alone or concurrently with parental training in behavior management, medication, or both	Office-based interventions produce minimal effects; some studies of behavioral peer interventions plus clinic-based parental training in behavior management showed positive effects on parental ratings of ADHD symptoms but no effects on social functioning	Combined with other approaches, so isolated effect size not determined	Effective programs also contain elements of parental training and behavioral classroom management	DuPaul et al. ⁴⁰

tion of medication use depends on its effects on behavior and function over time. As children approach adulthood, objectives shift increasingly toward social relationships, completing high school and receiving higher education, employment, and other relevant functional domains (Fig. 1 in the Supplementary Appendix).

Many studies show that children and adolescents switch forms of treatment over time and often discontinue the use of medication after 2 to 3 years.⁴⁴ Follow-up of the MTA cohort 6 to 8 years after the trial, when participants were 13 to 18 years of age, showed that the original study groups did not continue to receive their randomly assigned treatment and did not differ significantly from each other with respect to any variables, including grades, arrests, and psychiatric hospitalizations.⁶ The study participants fared worse on outcomes than local age-matched, normative comparison groups. The best predictors of functioning in adolescents were the severity of symptoms at enrollment, the socioeconomic status of the participant's family, and the degree of his or her response to any of the initial assigned study treatments.

AREAS OF UNCERTAINTY

Concerns have been raised about increased cardiovascular risk and decreased height after prolonged use of stimulant medication for ADHD. Although in 2008 the American Heart Association recommended electrocardiography in children before they begin to receive stimulant medications, subsequent studies showed that the frequency of unexpected death among children receiving stimulants was no higher than the frequency in the general population of children.^{45,46} Before stimulants are prescribed, it is prudent to inquire about the patient's cardiac history and family history of syncope or unexplained death.³⁴ A meta-analysis of cohort studies and clinical trials concluded that height attenuation with the use of stimulant medication is dose-dependent and is approximately 1 cm per year for up to 3 years of medication use. The amount of catch-up growth after discontinuation of medical therapy was inconsistent across studies.⁴⁷ Long-term studies are needed to assess the risks and benefits of ongoing treatment with medication.

Another area of uncertainty is whether vari-

ous broad-based interventions might reduce the prevalence or severity of ADHD.³⁸ Examples include training preschool children to use executive-function skills, such as response inhibition and working memory,⁴⁸ which has led to improvements in executive function at older ages; reducing noise in classrooms⁴⁹; and altering adverse factors associated with living in poverty, such as reducing food insecurity or increasing access to high-quality early education. Short- and long-term effects of interventions that target family, social, and environmental factors (e.g., increasing structure at home and school) also warrant evaluation.

A total of 12 to 64% of families with a child who has ADHD have reported the use of complementary and alternative therapies in their children. These therapies include dietary supplementation with essential fatty acids and high doses of vitamins, changes in diet, and electroencephalographic biofeedback.⁵⁰ The evidence is insufficient to recommend these therapies. Chelation and megavitamins may have adverse effects and are contraindicated.⁵¹ Careful study of new educational interventions, social-skills training, and life coaching is needed before these approaches can be recommended.

Adolescents who do not meet criteria for ADHD are increasingly using stimulant medications to improve cognitive skills (referred to as "neuroenhancement," though "performance enhancement" may be more accurate).⁵¹ Strategies are needed to ensure that stimulant medications are appropriately prescribed, used as directed, and not diverted for nonmedical use.

GUIDELINES

The AAP reissued practice guidelines for the diagnosis and management of ADHD,³⁶ highlighting differences in the treatment of preschool, school-age, and adolescent patients. A supplement to these guidelines provides information on how to ascertain the relevant data and engage the child in clinical care.³⁶ The American Academy of Child and Adolescent Psychiatry (AACAP) has also published guidelines for the diagnosis and management of ADHD.⁵² The AAP recommends direct contact between clinicians and teachers, whereas the AACAP permits parental reports of school performance. In addition, the AACAP recommends medication as first-line treat-

ment and psychosocial therapies if medication provides a less-than-satisfactory response, whereas the AAP promotes both types of management.

CONCLUSIONS AND RECOMMENDATIONS

The child described in the vignette has the core symptoms of ADHD — inattention, hyperactivity, and impulsivity — with functional impairment in academic performance and social relationships. He had improvement in core symptoms of ADHD when he received stimulant medication, as has been shown in randomized trials of these medications. However, the use of stimulants alone did not substantially improve his educational and social functioning. We recommend that the treating

physician suggest a comprehensive psychoeducational assessment to determine whether he has learning disabilities. In addition, his academic productivity and social difficulties should be targeted for interventions; given the demonstrated benefits of these methods in clinical studies, we would recommend behavioral parental training, behavioral classroom management, peer intervention approaches, or a combination of these methods. Specific, individualized, measurable objectives should be established and progress toward those objectives carefully monitored in collaboration with his family and teachers, as well as counselors, coaches, and other advisors in the community.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

- Diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV). Washington, DC: American Psychiatric Association, 2000.
- Diagnostic and statistical manual of mental disorders, fifth edition (DSM-5). Washington, DC: American Psychiatric Association, 2013.
- Biederman J, Petty CR, Woodworth KY, Lomedico A, Hyder LL, Faraone SV. Adult outcome of attention-deficit/hyperactivity disorder: a controlled 16-year follow-up study. *J Clin Psychiatry* 2012; 73:941-50.
- Loe IM, Feldman HM. Academic and educational outcomes of children with ADHD. *Ambul Pediatr* 2007;7:Suppl:82-90.
- Hoza B. Peer functioning in children with ADHD. *Ambul Pediatr* 2007;7:Suppl: 101-6.
- Molina BSG, Hinshaw SP, Swanson JM, et al. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry* 2009;48:484-500.
- Garcia CR, Bau CHD, Silva KL, et al. The burdened life of adults with ADHD: impairment beyond comorbidity. *Eur Psychiatry* 2012;27:309-13.
- Pelham WE, Foster EM, Robb JA. The economic impact of attention-deficit/hyperactivity disorder in children and adolescents. *J Pediatr Psychol* 2007;32:711-27.
- Pastor PN, Reuben CA. Diagnosed attention deficit hyperactivity disorder and learning disability: United States, 2004-2006. *Vital Health Stat* 10 2008;237:1-14.
- Boyle CA, Boulet S, Schieve LA, et al. Trends in the prevalence of developmental disabilities in US children, 1997-2008. *Pediatrics* 2011;127:1034-42.
- Fulton BD, Scheffler RM, Hinshaw SP, et al. National variation of ADHD diagnostic prevalence and medication use: health care providers and education policies. *Psychiatr Serv* 2009;60:1075-83.
- Schwarz A. The selling of attention deficit disorder. *New York Times*. December 14, 2013.
- Carlson CL, Mann M. Attention-deficit/hyperactivity disorder, predominantly inattentive subtype. *Child Adolesc Psychiatr Clin N Am* 2000;9:499-510.
- Neuman RJ, Sitdhiraksa N, Reich W, et al. Estimation of prevalence of DSM-IV and latent class-defined ADHD subtypes in a population-based sample of child and adolescent twins. *Twin Res Hum Genet* 2005;8:392-401. [Erratum, *Twin Res Hum Genet* 2005;8:542.]
- Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and meta-regression analysis. *Am J Psychiatry* 2007;164:942-8.
- Fergusson DM, Lynskey MT, Horwood LJ. Attentional difficulties in middle childhood and psychosocial outcomes in young adulthood. *J Child Psychol Psychiatry* 1997;38:633-44.
- Merrell C, Tymms PB. Inattention, hyperactivity and impulsiveness: their impact on academic achievement and progress. *Br J Educ Psychol* 2001;71:43-56.
- The ICD-10 classification of mental and behavioural disorders. Geneva: World Health Organization, 1993.
- Lee SI, Schachar RJ, Chen SX, et al. Predictive validity of DSM-IV and ICD-10 criteria for ADHD and hyperkinetic disorder. *J Child Psychol Psychiatry* 2008;49:70-8.
- Faraone SV, Mick E. Molecular genetics of attention deficit hyperactivity disorder. *Psychiatr Clin North Am* 2010;33:159-80.
- Braun JM, Kahn RS, Froehlich T, Auinger P, Lanphear BP. Exposures to environmental toxicants and attention deficit hyperactivity disorder in U.S. children. *Environ Health Perspect* 2006;114:1904-9.
- Froehlich TE, Anixt JS, Loe IM, Chirdkiatgumchai V, Kuan L, Gilman RC. Update on environmental risk factors for attention-deficit/hyperactivity disorder. *Curr Psychiatry Rep* 2011;13:333-44.
- Shaw P, Eckstrand K, Sharp W, et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. *Proc Natl Acad Sci U S A* 2007;104: 19649-54.
- Dickstein SG, Bannon K, Castellanos FX, Milham MP. The neural correlates of attention deficit hyperactivity disorder: an ALE meta-analysis. *J Child Psychol Psychiatry* 2006;47:1051-62.
- Castellanos FX, Proal E. Large-scale brain systems in ADHD: beyond the prefrontal-striatal model. *Trends Cogn Sci* 2012;16:17-26.
- Wolraich M, Brown L, Brown RT, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* 2011;128:1007-22.
- International classification of functioning, disability, and health (ICF). Geneva: World Health Organization, 2001.
- International classification of functioning, disability and health — version for children and youth: ICF-CY. Geneva: World Health Organization, 2007.
- Ustün TB. Using the international classification of functioning, disease and health in attention-deficit/hyperactivity disorder: separating the disease from its epiphenomena. *Ambul Pediatr* 2007;7:Suppl:132-9.

30. The medical home. *Pediatrics* 2002;110:184-6.
31. What is a family-centered medical home? Elk Grove Village, IL: American Academy of Pediatrics, 2005 (<http://www.medicalhomeinfo.org>).
32. Biederman J, Quinn D, Weiss M, et al. Efficacy and safety of Ritalin LA, a new, once daily, extended-release dosage form of methylphenidate, in children with attention deficit hyperactivity disorder. *Paediatr Drugs* 2003;5:833-41.
33. Faraone SV, Short EJ, Biederman J, Findling RL, Roe C, Manos MJ. Efficacy of Adderall and methylphenidate in attention deficit hyperactivity disorder: a drug-placebo and drug-drug response curve analysis of a naturalistic study. *Int J Neuropsychopharmacol* 2002;5:121-9.
34. Schachar R, Jadad AR, Gault M, et al. Attention-deficit hyperactivity disorder: critical appraisal of extended treatment studies. *Can J Psychiatry* 2002;47:337-48.
35. Efron D, Jarman F, Barker M. Methylphenidate versus dexamphetamine in children with attention deficit hyperactivity disorder: a double-blind, crossover trial. *Pediatrics* 1997;100:E6.
36. Subcommittee on Attention-Deficit/Hyperactivity Disorder Steering Committee on Quality Improvement Management. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* 2011;128:1-16.
37. Pelham WE Jr, Fabiano GA. Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. *J Clin Child Adolesc Psychol* 2008;37:184-214.
38. Antshel KM, Barkley R. Psychosocial interventions in attention deficit hyperactivity disorder. *Child Adolesc Psychiatr Clin N Am* 2008;17:421-37.
39. Parent training programs: insight for practitioners. Atlanta: Centers for Disease Control and Prevention, 2009.
40. DuPaul G, Eckert T, Vilaro B. The effects of school-based interventions for attention deficit/hyperactivity disorder: a meta-analysis 1996-2010. *School Psychol Rev* 2012;41:387-412.
41. The MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56:1073-86.
42. *Idem*. Moderators and mediators of treatment response for children with attention-deficit/hyperactivity disorder: the Multimodal Treatment Study of children with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56:1088-96.
43. Greenhill L, Kollins S, Abikoff H, et al. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. *J Am Acad Child Adolesc Psychiatry* 2006;45:1284-93. [Erratum, *J Am Acad Child Adolesc Psychiatry* 2007;46:141.]
44. Reid R, Hakendorf P, Prosser B. Use of psychostimulant medication for ADHD in South Australia. *J Am Acad Child Adolesc Psychiatry* 2002;41:906-13.
45. Perrin JM, Friedman RA, Knilans TK. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. *Pediatrics* 2008;122:451-3.
46. Cooper WO, Habel LA, Sox CM, et al. ADHD drugs and serious cardiovascular events in children and young adults. *N Engl J Med* 2011;365:1896-904.
47. Poulton A. Growth on stimulant medication; clarifying the confusion: a review. *Arch Dis Child* 2005;90:801-6.
48. Diamond A, Barnett WS, Thomas J, Munro S. Preschool program improves cognitive control. *Science* 2007;318:1387-8.
49. Clark C, Sörqvist P. A 3 year update on the influence of noise on performance and behavior. *Noise Health* 2012;14:292-6.
50. Weber W, Newmark S. Complementary and alternative medical therapies for attention-deficit/hyperactivity disorder and autism. *Pediatr Clin North Am* 2007;54:983-1006.
51. Graf WD, Nagel SK, Epstein LG, Miller G, Nass R, Larriviere D. Pediatric neuroenhancement: ethical, legal, social, and neurodevelopmental implications. *Neurology* 2013;80:1251-60.
52. Pliszka S. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2007;46:894-921.

Copyright © 2014 Massachusetts Medical Society.

SPECIALTIES AND TOPICS AT NEJM.ORG

Specialty pages at the *Journal's* website (NEJM.org) feature articles in cardiology, endocrinology, genetics, infectious disease, nephrology, pediatrics, and many other medical specialties. These pages, along with collections of articles on clinical and nonclinical topics, offer links to interactive and multimedia content and feature recently published articles as well as material from the NEJM archive (1812–1989).